

*Human
Subjects*

FS 48

Paper 10

TOLERANCE TO WHOLE-BODY IRRADIATION OF PATIENTS
WITH ADVANCED CANCER*

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1. PURPOSE

The purpose of this investigation was to determine the clinical and hematological effects upon human beings of daily repeated exposure of the entire body to filtered high-voltage x-rays in the Heublein unit for total-body irradiation.

2. FACTORS

The Heublein unit delivers x-rays generated at 180 to 185 kv, filtered through 1.10 mm Cu + 1.05 mm Fe or 1.65 mm Cu + 2.07 mm Fe in one room, and 1.10 mm Cu + 0.75 mm Fe or 1.65 mm Cu + 1.78 mm Fe in the other room. In either room the thicker filter provides 0.85 r per hour while the thinner filter provides 1.65 r per hour. The average target-to-body distance is about 300 cm.

It was requested that first some patients be treated with a dose of 10 r per day for 30 days, then some at 15 r per day for 20 days, then, if possible, some at 20 r per day for 15 days. This total dose of 300 r was arbitrarily selected on the basis of previous experience, from 1931 to 1933 and from 1935 to 1942, with the Heublein unit. On the basis of that experience it was believed that 300 r could be tolerated in one course of treatment over a period of 10 to 30 days by individuals in good general condition and that it should be a sufficient dose to yield some detectable effects on the blood count and to serve as a guide to the clinical tolerance for whole-body irradiation.

*Based on Metallurgical Laboratory Report CH-3369.

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3. SELECTION OF PATIENTS

This was the most difficult part of the project, calling for the selection of patients having metastatic cancer of such extent and distribution as to render their cases totally unsuitable for any accepted method of surgical or radiological treatment, yet demanding that the patients be in good enough general condition so that they might be expected not only to tolerate the exposure to 300 r of total-body irradiation in a period of 10 to 30 days, but also to survive the combined effects of their disease and the irradiation for at least six months in order that some conclusions might be drawn as to the later effects of the irradiation.

It was recognized that none of the patients with lymphomas or leukemias would be suitable for this project because of the sensitivity of the hematopoietic system in such cases both to irradiation and to various disorders incidental to the disease. Thus it was necessary to confine the selection to subjects with metastatic carcinomas and metastatic sarcomas other than of the lymphoid system.

It was recognized, moreover, that in such advanced cases the further progress of the malignant neoplastic process, if indeed it did not cause the death of the patient sooner than six months after whole-body irradiation, would in any case be very likely to confuse the interpretation of the clinical and hematological effects of irradiation by reason either of changes in the patient's nutrition or other alterations attributable to the disease. However, it could be argued that if it were possible to show that no definite or marked harm resulted in patients as sick as those to be chosen, it could certainly be concluded that healthy persons should be able to tolerate the projected dose of irradiation.

The hope that, despite the negative results obtained in 1931 in cases of radioresistant metastatic cancer by use of doses of up to 450 r in the Heublein unit there might nevertheless on further trial be found some beneficial clinical effect, offered justification, in addition to the primary purpose, for undertaking the project.

4. METHOD

Carefully selected patients were admitted to the Heublein unit, where they received the prescribed daily dose of whole-body irradiation day after day without interruption. During the treatment a complete blood count, including a differential and platelet count, was made every 2 to 4 days. Upon completion of the treatment the patients were as a rule able to go home at once and were then seen at intervals of

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at 10 r per day given nineteen months previously, could have been responsible in any way for this improvement; and, per contram, it is a matter for speculation as to whether the patient's bedridden state, occurring for eight months following the irradiation and causing him

and who may year after to rioid, although temporarily basis it might in case 6 was blood counts his home.

Table 10.1 — Patients Treated between Dec. 18, 1942, and Aug. 29, 1944

Case no.	Sex	Age	Diagnosis	r/day	Dose total,	End result
					r	
1	M	31	Melanoma	10	300	Died at home, from progress of disease, 31 days after treatment
2	M	25	Teratoma testis, metastasis to lungs	10	150	Died in hospital, from progress of disease, 71 days after treatment
3	M	44	Melanoma	10	161	Died at home, from progress of disease, 49 days after treatment
4	F	52	Carcinoma of breast	10	300	Last seen 4 months 4 days after treatment; probably died soon afterward
5	M	64	Carcinoma of male breast	10	300	Living 18 months after treatment, but had orchiectomy 1 year after treatment
6	M	33	Pulmonary metastases of mucoepidermoid carcinoma of parotid	10	300	Living 19 months after treatment; bedridden from 8 months after treatment until about 17 months after treatment; then gained 25 pounds and became ambulant
7	M	46	Metastatic adenocarcinoma, primary undetermined	15	300	Followed 4½ months after treatment; was then in a terminal institution
8	M	51	Metastatic adenocarcinoma (primary in sigmoid?)	15	300	Last seen 7¼ months after treatment; going to a terminal institution; extensive liver metastases when last seen

Date	HGB
12/9/42	92
12/15/42	74
12/18/42	97
12/19/42	100
12/21/42	75
12/24/42	80
12/28/42	78
12/31/42	80
1/4/43	79
1/8/43	80
1/8/43	77
1/11/43	80
1/13/43	80
1/20/43	94
1/26/43	93
2/2/43	68
2/28/43	Died

to be unable to return for eleven months, was a late effect of the irradiation, an effect from which he was recovering. The only other patient followed for a comparable time was the patient with male-breast carcinoma followed for eighteen months, who continued at work

7.1 Case of skin of metastases. Only eight months: Between 1 rate of 10 r During treatment, although following treatment, white cells and a drop 142,000 to 3 In the two pletion of t

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Toward the end of the period of treatment and for six weeks afterward there was a trend toward a decreased level of hemoglobin, red cells, and white cells. However, considering the wide extent of the patient's metastatic cancer, it is quite possible and perhaps more probable that these blood changes were caused by the disease rather than by the treatment.

Table 10.9—Case 8, Age 51, Carcinoma (of Sigmoid?) Metastatic Adenocarcinoma in Supraclavicular Nodes

Date	HGB	RBC	WBC	Polys	Eos	Baso	Mono	Lymph	Misc	Plat (1,000)	Retic
7/3/44	90	4.48	8.0	68				32		215	
8/7/44	75	3.7	13.4	69			2	29		Normal	
8/9/44	80	4.0	10.0	66			4	30		128	
8/12/44	75	3.7	9.0	64			3	33		118	
8/14/44	80	4.0	10.8	72			6	22		Decreased	
8/16/44	74	3.6	8.2	70			4	26			
8/19/44	77	3.8	10.3	70			10	20			
8/21/44	80	4.1	7.6	84			8	8			
8/24/44	77	3.7	6.8	70			10	20		179	
8/26/44	80	4.0	9.4	80			8	14			
8/28/44	83	4.2	8.2	80			6	14		Decreased	
9/6/44	78	3.9	8.4	78			12	10			
9/20/44	70	3.5	3.4	78			18	6		94.8	
11/12/44	78	3.9	9.8	82	2		8	28		218	
12/15/44	67	3.9	11.6	81				19		131.3	
1/12/45	80	3.7	10.2	69				31		286	
1/26/45	85	4.0	7.0	70				30		98	
2/23/45	84	4.3	5.2	69			6	25		263	
4/6/45	69	3.4	9.0	83			3	14		109	

After six weeks following treatment the patient was not seen again at Memorial Hospital. He was admitted to a terminal institution on July 12, 1944.

7.8 Case 8, Male, Age Fifty-one Years. Diagnosis: Metastatic adenocarcinoma of supraclavicular nodes (primary in sigmoid?) No previous irradiation.

Between Aug. 8 and 29, 1944, received 15 r per day for 20 days. No consistent change was noted in blood counts during or following the treatment which might not be attributed either to the disease or to technical errors. (Rather wide variations were reported.)

The case was followed until Apr. 6, 1945, a little over seven months after treatment. At that time the patient was admitted to a terminal institution.

8. SUMMARY

1. Eight patients having advanced metastatic cancer were exposed to heavily filtered 180 kv x-rays in the Heublein unit at hourly inten-

sities of 0.85 or 1.65 r and for daily doses of 10 or 15 r up to the projected total dose of 300 r delivered in either 20 or 30 days.

2. The projected total dose, 300 r, was attained in six cases. In two cases (cases 2 and 3) in which the total desired dose was not attained, the treatment was discontinued at 150 and 161 r, respectively, because of progress of the disease; and the disease caused death in 71 and 49 days, respectively, afterward.

3. The projected minimum of six months of follow-up examination, clinical and hematological, subsequent to exposure to total-body irradiation was attained in three of the eight cases (cases 5, 6, and 8). In cases 1, 4, and 7, although the total projected dose, 300 r, was administered, the progress of the cancer caused the cases to be lost to routine follow-up in from one to four months.

4. In no case did there occur any deterioration in the blood count that might not reasonably be ascribed to the progress or complications of the malignant neoplasm.

5. In the three cases followed for longer than six months (seven and one-quarter to nineteen months) there was no deterioration in general health not reasonably attributable entirely to the progress of the disease.

6. In one case (case 6) followed for nineteen months, a remarkable improvement took place in the seventeenth month after treatment. The improvement is not credited to the treatment.

7. In no instance was there observed any suggestion of stimulation of growth of neoplasm by the whole-body exposure to radiation.

Data gathered from previous experience (1931 to 1933 and 1935 to 1942) with administration of whole-body roentgen therapy, involving doses of from 5 to 450 r, agree essentially with the findings reported in this paper, although in cases of lymphoma and leukemia unfavorable clinical and hematological results were observed in some instances.

9. CONCLUSIONS

In eight cases of advanced metastatic malignant neoplasm in human beings, exposure of the entire body to 180 kv heavily filtered x-rays at an intensity of 10 r per day (0.85 r per hour) or 15 r per day (1.65 r per hour), for total doses of 150 and 161 r in two cases and 300 r in six cases, was not followed by clinical or hematological effects ascribable to the radiation, either during or within a month after cessation of exposure.

In five cases followed for from four to nineteen months after exposure there was, likewise, no deterioration in blood count or clinical state that could not reasonably be ascribed entirely to the progress of the neoplastic disease.

It seems proper to conclude, therefore, on the basis of these few cases, that since individuals so seriously ill of cancer could withstand up to 300 r of total-body 180 kv heavily filtered roentgen exposure, administered in a period of from 20 to 30 days, with no appearance of subsequent ill effects other than those apparently caused by the progress of the disease, such doses of radiation should be well tolerated by healthy persons.